PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	25.05.2004
Applicant's or agent's file reference	**IMPORTANT NOTIFICATION**
SCB746PCT	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP 03/00078	07.01.2003	11.01.2002

Applicant
FIDIA FARMACEUTICI S.P.A. et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
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PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference SCB746PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP 03/00078	International filing date *(day/month/year)* 07.01.2003	Priority date *(day/month/year)* 11.01.2002
International Patent Classification (IPC) or both national classification and IPC A61L27/00, A61L27/00		
Applicant FIDIA FARMACEUTICI S.P.A. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
23.07.2003	25.05.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Heller, D Telephone No. +49 89 2399-8746

The use of the biomaterial for the treatment of cancer as claimed in claims 1 to 9 is also already known from the following documents with their cited passages:
Even if D7 discloses the use of amides and is therefore not relevant concerning novelty vis-à-vis the benzyl ester of hyaluronic acid, hyaluronic acid esters are used to prepare amides which can be cross-linked (p. 4, ll. 14ff). Such a cross-linking falls within the scope of claim 1, the cross-linked derivatives of HA. Therefore, present claims 1 to 9 are not novel over D7 (see p. 1, ll. 11 - 14; claims 1, 5, 16, 21, 23).
The same applies for D8 (see claims 1-31) and D11 (see p. 3, ll. 35-47; p. 7, ll. 28-31).
D10 (see col. 1, ll. 6-12; claims 1-8, 25) discloses the esters of HA even benzyl esters for the same treatment.

Inventive step

Even if the applicant is able to establish novelty it cannot be seen that any particular aspect of the application as filed would involve an inventive step under Article 33 (3) PCT in the light of the relevant prior art.

Priority

The applicant is informed that no check has been made as to whether priority has been validly claimed. Therefore, documents D1 to D3 (WO02/18448; WO02/41877; WO02/18450), which have been disregarded in writing the present opinion, could become relevant for the assessment of novelty once the present application enters the regional phase (Rule 64 (1) b PCT).

End. 1

CLAIMS

1. **Use of benzyl ester of** hyaluronic acid or **a cross-linked derivative of hyaluronic acid wherein the carboxy groups of hyaluronic acid are cross-linked to the hydroxyl group of the same or different hyaluronic acid molecule,** for the preparation of a **biomaterial** suitable for antiangiogenic therapy to treat primary and secondary tumours.

2. **The use according to claim 1** wherein hyaluronic acid is in association with other natural, synthetic and/or semisynthetic biopolymers.

3. The use according to claim 2, wherein the natural biopolymer is selected from the group consisting of collagen, cellulose, polysaccharides, chitin, chitosan, pectins, agar, gellan and alginic acid.

4. The use according to claim 2, wherein the synthetic biopolymer is selected from the group consisting of polylactic acid (PLA), polyglycolic acid (PGA), polyurethanes and polysulphonic resins.

5. The use according to claim 2, wherein the semisynthetic biopolymer is selected from the group consisting of collagen cross-linked with aldehydes, diamine and gellan.

6. The use according to claim 1 wherein the biomaterial is associated with pharmacologically active substances.

7. The use according to claim 6, wherein the pharmacologically active substance **is selected from the group consisting of** fluorouracil, methotrexate, cis-platinum, carboplatin, oxaliplatin, ethopoxide, cyclophosphamide, vincristine, doxorubicin.

8. The use according to any one of claims 1-7 wherein the biomaterial is in the form of a non-woven felt, sponge, microsphere, film or membrane and/or other three-dimensional structures.

9. The use according to any one of claims 1-8, for the treatment and care of primary and secondary tumours when the tumour has been surgically removed and the cavity that is thus formed requires filling.